

AMENDMENTS TO THE CLAIMS

1 - 30 (cancelled)

31. (withdrawn) A method of positively identifying viable, expanded or passaged, committed, pluripotent skeletal precursor cells that have entered a post-natal differentiation pathway leading to skeletal or connective tissues comprising the steps of isolating mammalian cells into a cell culture in vitro, and detecting the presence of a positive embryonic marker of an expressed bone morphogenic or cartilage derived morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker.

32. (withdrawn) The method according to claim 31, wherein the presence of the positive marker is further characterized by the absence of a negative marker, said negative marker preferably being FGFR3 or a marker or factor co-expressed or co-detectable with this negative marker.

33. (withdrawn) The method according to claim 31 wherein the positive marker is an actively expressing gene, a protein or an mRNA expressed by a gene in the precursor cells or a part thereof, detectable at the DNA, mRNA, cDNA or the protein level and/or

detectable via the activity of a promoter directing/regulating this gene expression, operably linked to heterologous reporter gene.

34. (withdrawn) The method according to claim 31 wherein the positive marker identifies precursor cells of a joint interzone in mammals.

35. (withdrawn) The method according to claim 31 wherein the expressed bone morphogenic or cartilage derived morphogenic protein is the cartilage-derived morphogenic protein CDMP-1 or a transforming growth factor b having at least 80% homology with CDMP-1 as a marker of skeletal precursor cells from any part of the body or a marker or factor co-expressed or co-detectable with any or all of these positive markers.

36. (withdrawn) A method according to claim 31, wherein the step of detecting the presence of the positive marker includes applying a binding agent for the positive marker to an isolated source of cell having the precursor cells, the marker positively identifying the cell and separating the cells which are bound to the binding agent.

37. (withdrawn) A method for sorting and/or enriching precursor cells in cell culture in vitro comprising selecting cells with reagents, ligands, and/or monoclonal or polyclonal

antibodies recognizing cell surface markers wherein the cell surface marker is co-expressed or co-detectable with the marker of claim 31, said precursor cells optionally being skeletal precursor cells.

38. (withdrawn) A method for producing or repairing connective tissue into a mammal comprising administering skeletal precursor cells marked according to claim 31, said cells optionally being cultured at a cell density of at least 10^5 cells/ml and/or having a factor administered that stimulates differentiation of the skeletal precursor cells in the type of connective tissue to be produced or repaired.

39. (withdrawn) A method of producing matrix comprising cultivating precursor cells marked according to claim 31 as matrix producing cells, said matrix optionally further comprising a bioresorbable polymer or carrier.

40. (withdrawn) A method for treating subglottic stenosis, tracheomalacia, chondromalacia patellae, osteoarthritis and traumatic lesions in a mammal said method comprising supplying precursor cells being marked according to claim 31.

41. (withdrawn) A method for joint surface defect repair in a mammal comprising the co-implantation of chondrocytes and skeletal precursor cells marked according to claim 31.

42. (withdrawn) A method for enhancing the implantation of a prosthetic device in connective tissue comprising the step of implanting a prosthetic device having skeletal precursor cells according to claim 31 adhered thereto under conditions suitable for differentiating the cells into the connective tissue desired, method of treatment.

43. (currently amended) ~~A~~ purified culture of ~~isolated and expanded~~ viable, differentiated, ~~pluripotent~~ precursor cells isolated from periosteum, bone marrow, or synovial membrane, that have entered a post-natal skeletal differentiation pathway leading to skeletal or connective tissue, wherein the cells express a positive embryonic marker which is CDMP-1 or a marker co-expressed and/or co-detectable with CDMP-1.

44. (currently amended) A therapeutic composition comprising a culture of ~~isolated and expanded~~ viable, differentiated, ~~pluripotent~~ precursor cells, isolated from periosteum, bone marrow, or synovial membrane and expanded, that have entered a post-natal skeletal differentiation pathway leading to skeletal or connective tissue, wherein the cells express

a positive embryonic marker which is CDMP-1 or a marker co-expressed and/or co-detectable with ~~said embryonic marker~~CDMP-1.

45. (previously presented) An implant comprising the cells of claim 43, said implant being optionally suitable for connective tissue implantation.

46. (withdrawn) A method of treating a patient in need thereof comprising the step of administering the therapeutic composition of claim 44 to said patient.

47. (withdrawn) A diagnostic for positively identifying in vitro a positive marker of viable, committed, pluripotent skeletal precursor cells that have entered a post natal differentiation pathway leading to skeletal or connective tissues, wherein the marker is an expressed bone morphogenic or cartilage derived morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker.

48. (withdrawn) The diagnostic according to claim 47 wherein the diagnostic also identifies the absence of a negative marker.

49. (withdrawn) The diagnostic according to claim 47 wherein the positive marker identifies precursor cells of a joint interzone in mammals.

50. (withdrawn) The diagnostic according to claim 47 wherein the expressed bone morphogenic or cartilage derived morphogenic protein is the cartilage derived morphogenic protein CDMP-1 or a transforming growth factor beta having at least 80 % homology with CDMP1 as a marker of skeletal precursor cells from any part of the body or a marker or factor co-expressed or co-detectable with any or all of these positive markers.

51. (withdrawn) A method to positively identify viable committed skeletal pluripotent precursor cells that have entered a post natal differentiation pathway leading to connective or skeletal tissues, comprising selecting or identifying cells expressing an embryonic marker wherein the embryonic marker is an expressed bone morphogenic or cartilage derived morphogenic protein, a homolog thereof or a marker co-expressed and or co-detectable with this marker.

52. (withdrawn) A method for producing or repairing a connective tissue in a mammal comprising the step of administering to said mammal the therapeutic composition of claim 44.

53. (withdrawn) The method according to claim 52, said method comprising administering the composition at a cell density of at least 10^5 cells/ml and administering a factor that stimulates differentiation of the cells of the composition in the connective tissue.

54. (withdrawn) The method according to claim 52, said method comprising administering the cells of the composition at a cell density of at least 10^5 cells/ml.

55. (withdrawn) The method according to claim 52, said method comprising administering a factor that stimulates differentiation of the cells of the composition in the connective tissue.

56. (withdrawn) A method of producing matrix comprising the step of cultivating the therapeutic composition of claim 44 as matrix producing cells, said matrix optionally further comprising a bioresorbable polymer or carrier.

57. (withdrawn) A method for treating subglottic stenosis, tracheomalacia, chondromalacia patellae, osteoarthritis or traumatic lesions in a mammal said method comprising the step of supplying to said mammal the therapeutic composition of claim 44.

58. (withdrawn) A method for joint surface defect repair in a mammal comprising the step of co-implanting, in said mammal, chondrocytes and the therapeutic composition of claim 44.

59. (withdrawn) A method for enhancing the implantation of a prosthetic device in connective tissue comprising the step of implanting, in a mammal, a prosthetic device having the therapeutic composition of claim 44 adhered thereto under conditions suitable for differentiating the cells of said composition into connective tissue.

60. (cancelled)

61. (currently amended) The therapeutic composition of claim 44, wherein said ~~expanded-viable, differentiated, pluripotent~~ precursor cells that have entered a post-natal skeletal differentiation pathway leading to skeletal or connective tissue are further characterized by the absence of a negative marker, said negative marker being FGFR3 or another marker or factor co-expressed or co-detectable with said FGFR3 of the mature chondrocyte phenotype.

62. (cancelled)

63. (new) The therapeutic composition of claim 44, which further comprises a chondrocyte cell population.

64. (new) The culture of claim 43, wherein said viable, differentiated precursor cells are further characterized by the absence of a negative marker, said negative marker being FGFR3 or another marker of the mature chondrocyte phenotype.